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| 10/560,821 | 12/15/2005 | Tsunenori Arai | 011350-367 | 9015 |

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| EXAMINER | |
|---|---|
| SHAY, DAVID M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 3769 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 06/10/2009 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/560,821 | ARAI ET AL. | |
| | Examiner | Art Unit | |
| | david shay | 3769 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *April 24, 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-18 and 22-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 22-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *April 24, 2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 20, 2009 has been entered.

Applicant has chosen to amend the specification by filing a substitute specification, apparently under 37 C.F.R. 1.125(b), however, the requirements of 37 C.F.R. 1.125(b) have not been fully complied with, in that the specification has not been accompanied by a statement that it contains no new matter. Therefore, the substitute specification is improper and has not been entered.

The drawings are objected to because elements 11, 12, 13, 14, and 20-24 in Figure 4 are not labeled with indicia indicative of their function. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not

accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, the "input means for being input a preserved distance" and the "controlling not to activate the photosensitive substance in the superficial part of the body located close to the light irradiation means then the lesioned part" must be shown or the feature(s) canceled from the claim(s). No new matter should be entered.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

It is noted that the term: "input means for being input a preserved distance" satisfies the three pronged test for a means plus function recitation and with be treated as such herein. See MPEP 2181(I)

The amendment filed February 17, 2009 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: "input means for being input a preserved distance".

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant expresses confusion with respect to the examiner's objection to the 35 U.S.C. 112, first paragraph, requires the specification to be written in "full, clear, concise, and exact terms." The revision provided failed to yield a specification that meets the requirement. Many portions are unclear due to non-standard or contradictory terms and phrases, as well as terms and phrases that appear to be synonyms, but are used as though their definitions are different and

distinct. One specific term is peak intensity that has multiple values; i.e. low peak intensity and high peak intensity as explained above. By definition peak is "the maximum value of a quantity during a specified time interval: a voltage peak". Thus the terms low peak and high peak in the disclosure are improper and confusing. Another example are the terms "cell fatality rate" and "cell death rate" "fatality" is defined by Webster's dictionary as "the quality of causing death or destruction" thus it is unclear how the two terms are =to be construed as representing different concepts. The specification must be clear such that multiple interpretations of the invention do not result. The specification is replete with missing pronouns and tense errors that hinder clear understanding of the invention.

Claims 13 and 29 cite achieving the peak intensity of the predetermined range. That would be, by definition, the highest intensity of the range. The examiner believes the intent was to achieve an intensity within the predetermined range. This highlights a concern with the term peak intensity throughout the disclosure.

With regard to the enablement rejection, applicant traverses, citing a passage on page 17 of the originally filed disclosure. The examiner must respectfully note that this information is insufficient to provide the claimed device with the capability of controlling the irradiation of a lesion which is at un unknown depth or size, or is at a varying depth from the surface of light impingement, thus this argument s not convincing. With regard to claim 17, while certain parameters my be determinable empirically, as applicant argues, this does not enable a "control means **calculating** and irradiation condition…" as claimed in claim 17. Thus this argument is not convincing.

With regard to the indefiniteness rejection, the standard by which one of ordinary skill in the art would determine that a given intensity was a "high peak intensity" or a "low peak intensity" is not clear, thus this argument is not convincing.

With regard to the anticipation and obviousness rejections, applicant argues the intended use of the device, rather than the structure positively recited in the claim. To the extent that applicant is arguing that the intended use recited in claims 1 and 17 is not be disclosed in Parker et al, the examiner notes that claims 1 and 17 are apparatus claims and absent some structure which expresses this intended use, Parker et al still reads on the claims.

Applicant's arguments filed February 17, 2009 have been fully considered but they are not persuasive. The irradiated light may only have one peak intensity. By definition peak is "the maximum value of a quantity during a specified time interval: a voltage peak". Thus the terms low peak and high peak in the disclosure are improper and confusing. The examiner interprets the intent is that a range of intensities exists that provide optimal PDT, that range having a low intensity value and a high intensity value. The positively cited limitations of the apparatus claims are a light irradiating means and a control means, both of which are clearly anticipated by Parker et al. The functional language does not clearly indicate how the many variables required to properly control to a specific depth are determined or communicated to the controller, although such inputs would be obvious to a skilled artisan as indicated by Dougherty and Dumoulin-White et al. herein. Thus, the control means is interpreted as being capable of controlling as per the functional language. The microprocessor of Parker et al. meets that interpretation.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 26-28 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 26 positively recites the tissue.

Claims 1-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The control means is enabled to control the operational parameters of the light. The depth in a body where the photosensitizer is activated is a result of the light intensity reaching the photosensitizer and the wavelength of the light. The activation is dependent on the characteristics of the photosensitizer. The irradiation intensity at a target depth is dependent on the attenuation of the light by the tissue and vessels. The control means is not enabled to process these variables. Further the "input means for being input a preserved distance" is not described by substantial materials, acts, or structure in the originally filed disclosure, and is thus not enabled (see MPEP 2185).

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Means for "controlling not to activate the photosensitive substance in the superficial part of the body located close to the light irradiation means then the lesioned part" is not enablingly disclosed. It is unclear how the part of the body that the light hits fist, when it is at it's greatest intensity, before being absorbed and or scattered by both the photosensitizer and tissue in the superficial part can, at the same time, be

insufficient to activate the photosensitizer in the superficial tissue, yet be intense enough to activate the photosensitizer which is at a deeper level in the tissue.

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Means for measuring the cell death rate and providing same to a controller for calculation of control parameters is not disclosed. Without providing a cell death rate to the control means, no calculation based on that variable is possible.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. "input means for being input a preserved distance" is new matter.

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. A control means calculating an irradiation condition based on measurement of result of rate of cell death is new matter.

Claims 1-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 13, 17 and 29 recite the limitations "peak intensity", "high peak intensity", and "peak intensity range". The terms are not clearly defined in that a peak intensity, by definition, must have a single peak intensity. The term "high peak intensity" is unclear as high can be interpreted as a relative term and what constitutes a "low peak intensity" which is not encompassed by the term "high peak intensity" is unclear. Further, claims 1, 13, 17 and 29 are incomplete, as they provide no means or steps by which the intensity of the light at certain depths for any general tissue is sensed or determined. Still further, claim 1 is indefinite, as it provides no substantial materials, acts, or structure means by which the "input means for being input a preserved distance" is to be implemented (see MPOEP 2185); and the meaning of the term "input means for being input a preserved distance" is unclear. Claim 1 recites the limitation "input means for being input a preserved distance" in line 5. There is insufficient antecedent basis in the originally filed disclosure for this limitation in the claim. Claim 10 is unclear as the term "not changing the total number of pulse of the light irradiated from the irradiation means , but by controlling the peak intensity of the light" is not clear as it lacks positive antecedent basis in the originally filed disclosure. Claim 11 is indefinite as directed to intended use. The total energy is related to intensity over time and therefore is dependent on the time of treatment. Claim 12 is unclear as a peak intensity has, by definition, a single value, yet the peak intensity is cited as changing. Claim 13 recites the limitation "the photodynamic therapy" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 13 recites the limitation "the

wavelength" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim. Claims 13 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: determination of tissue type or attenuation properties of the tissue and a determination of the boundaries of the target and non-target areas. The depth limits of the superficial part would be required inputs for an intensity calculation. In claim 14, "the repetition frequency" lacks positive antecedent basis. In claim 16, it is unclear which of the peaks, the high peak intensity or the low peak intensity is "the predetermined range". Claim 17 is indefinite due to the term "and controls a rate of cell death damaged by...". It's the photosensitizer to kill or damage the cells? Claim 18 is indefinite as the term "total number of a irradiation pulse" is not clear. Claim 22 recites the limitation "the cell fatality rate" in line 3. There is insufficient antecedent basis for this limitation in the claim, further the claim is indefinite because it is unclear what, if any further limitation is recited thereby, as it is unclear what the difference between "the rate of cell death" and "the cell fatality rate" as these appear to be the same thing, and thus how one is controlled to be above the other is unclear, the disclosure at paragraph [0079] of the PGPub, also the last full paragraph on page 19 of the originally filed disclosure, which appears to assert a difference therebetween but does not articulate such difference in a manner understandable to the examiner, notwithstanding. Claim 23 is indefinite as the term "total number of the irradiation pulse" is not clear. Claim 23 recites the limitation "the cell fatality rate" in line 4. There is insufficient antecedent basis for this limitation in the claim. Claim 24 is unclear as a peak intensity has, by definition, a single value, yet the peak intensity is cited as controlled or changing. Claim 24 recites the limitation "the cell fatality rate"

in line 4. There is insufficient antecedent basis for this limitation in the claim. Claim 25 recites the limitation "the cell fatality rate" in line 4. There is insufficient antecedent basis for this limitation in the claim. Claim 29 recites the limitation "the high peak intensity" in line 13. There is insufficient antecedent basis for this limitation in the claim.

Claims 1, 2, 4-6, 10-12, 17 and 22-25 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 4,592,361 to Parker et al.

Parker et al. disclose an apparatus for delivering photodynamic therapy with a pulsed light source (Fig. 3, # 16) having a wavelength, intensity, pulse width and pulse rate controlled by a microprocessor (Col. 12, lines 3-14). Thus, the device is capable of controlling (control means) the intensity based on inputs to the microprocessor. The language regarding the depth of photosensitizer and activation has no defined structure, but is related to the intended use of selectively activating the photosensitizer at a desired target.

Claim 1 only positively claims a controlled irradiation means and an "input means for being input a preserved distance". Parker et al. is capable of directing light of an intensity and pulse rate at a target area. How the light behaves in the tissue is dependent on the photosensitizer used, wavelength (a primary determinate of penetration depth), intensity and tissue properties. Altering the intensity (peak intensity) is clearly part of a control process. The microprocessor control of Parker et al. is capable altering the parameters as discussed above as required by the photosensitizer being used as is well known in the arts. Lacking specific structural limitations other than control means and irradiation means fails to provide finite metes and bounds and allows Parker et al. to be broadly interpreted to read on the claims. The box-car untegrator is considered to be "input means for being input a preserved distance" to the extent the examiner

can ascribe a meaning to this term in the context of the instant specification. Regarding claim 5, Parker et al. teach controlling the irradiation source using a detector to determine the level of oxygen available to avoid depletion that would inhibit singlet oxygen production (Col. 13, lines 25-35). Regarding claim 6, Parker et al. disclose the light may be an Nd:YAG laser operating at a second harmonic (Col. 10, line 18). The controller of Parker et al. is capable of controlling the parameters of the laser Regarding claim 29, Parker et al. discloses detecting fluorescence from a photosensitizing dye, thus it is inherent that such would have to be administered and irradiation is clearly done with the structure disclosed.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 4,592,361 to Parker et al. as applied to claim 1 above and further in view of U.S. Patent Application Publication US 2003/0022105 to Prasad et al. Parker et al. are discussed above, but do not teach intensities or pulse rates. Prasad et al. discloses intensities for photodynamic therapy of from 0 to 200 MW/cm2 (paragraph 0321) and pulse rates of from 0.1 Hz to 1 kHz (paragraph 0334). Control of light parameters in photodynamic therapy is pervasive in the art and, therefore, it would have been obvious to one skilled in the art to use the intensities and pulse rates as taught by Prasad et al. in the device of Parker et al. to obtain the light parameters required for a specific photosensitizer.

Claims 7-9 and 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 4,592,361 to Parker et al. as applied to claims 1 and 17 above and further in view of U.S. Patent 5,514,669 to Selman. Parker et al. are discussed above, but do not teach the use of a catheter for delivery of light for photodynamic treatment. Selman teaches photodynamic therapy wherein the light energy is delivered to a patient's prostate by placing the light delivery means in

a urethral catheter. The light delivery means is properly located within the urethra and positioned adjacent to the target prostate tissue. A balloon may be affixed to the distal end of the catheter (Col. 5, lines 15-25). It would have been obvious to one skilled in the art to use the catheter as taught by Selman in the device of Parker et al. as the use of such catheters is pervasive in the arts.

Claims 13-16 and 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 4,592,361 to Parker et al. in view of U.S. Patent 6,413,267 to Dumoulin-White et al. and U.S. Patent 5,145,863 to Dougherty. Parker et al. are discussed above, but do not teach methodology for achieving an intensity at a specific depth in tissue. Dougherty teaches a method for destroying cells using photoradiation of target tissue with a photosensitizer, wherein a specific depth is known and the intensity determined for specific depths, which are considered to be a "preserved distance". With the attenuation constant known, the depth of penetration of a minimum irradiance or conversely the required irradiance for a minimum intensity at a given distance may be calculated. (Col. 18, lines 49-54). Dumoulin-White et al. disclose a method to estimate the depth dependence of intensity (i.e., the attenuation of intensity as a function of depth) in tissue being treated. For example, the radial dependence can be used to generate a curve or formula for a curve, which can in turn be used to select a depth dependence curve or formula from a look-up table. In any event, the intensity (or irradiance) of radiation at target depth is determined from the depth dependence curve or formula, and the radiant exposure at target depth is determined by, e.g., integration (Col. 5, lines 40-49). An inherent feature of all photosensitizers is a range of activation. It would have been obvious to one skilled in the art to use the techniques for determining an intensity at specific depths in tissue as taught by

Dougherty and Dumoulin-White et al. to control the radiation of Parker et al. to control a photodynamic process. A skilled artisan would know the activation characteristics of the photosensitizer used and the depths to be treated and would be motivated to insure the proper intensity required was delivery at the proper location or locations. Regarding claim 30, the various methods for delivery of a photosensitizer and well known in the art (see Selman cited above).

Applicant's arguments filed February 17, 2009 have been fully considered but they are not persuasive. The arguments are not persuasive for the reasons set forth above.

Applicant's arguments with respect to claims 1-18 and 22-30 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to david shay whose telephone number is (571) 272-4773. The examiner can normally be reached on Tuesday through Friday from 6:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Henry Johnson, can be reached on Monday through Friday from 7:00 a.m. to 3:30 p.m. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/david shay/

Primary Examiner, Art Unit 3769